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10/525,158	02/22/2005	Tsuneo Yasuma	66585(70820)	5896

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EXAMINER	
MOORE, SUSANNA	
ART UNIT	**PAPER NUMBER**
1624	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,158	YASUMA ET AL.	
	Examiner	Art Unit	
	SUSANNA MOORE	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4-6,8-20,28,29,32,33 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4-6,8-18,28,29,32,33 and 35* is/are rejected.

7)☒ Claim(s) *19 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/29/07,12/19/05,3/14/05,2/22/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Group I in the reply filed on 11/19/2007 is acknowledged. Group I is the compounds of formula I drawn to pyrazolo[1,5-a]pyrimidines. Applicants pointed to no errors in the Examiners analysis of the classification of the different inventions. The requirement is still deemed proper and is therefore made **FINAL**.

This action is in response to a restriction requirement filed on 10/19/07. There are 25 claims pending and 25 under consideration. Claims 2, 4-6, 8-20, 32, 33 and 35 are compound and composition claims. Claims 28 and 29 are method of using claims. This is the first action on the merits. The application concerns substituted pyrazolo[1,5-a]pyrimidines, and uses thereof.

This application contains claims drawn to an invention nonelected with traverse. A complete reply to the Office Action must include cancellation of nonelected subject matter or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Substituted Pyrazolo[1,5-a]pyrimidines as Calcium Receptor Modulating Agents.

Claim Objections

Claims 19 and 20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 4-6, 8-18, 32, 33 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 12 have a proviso directed to R^9 and R^{10}. The proviso states that at least one of R^9 and R^{10} is $CHR^{15}R^{16}$. However, the definitions of R^9 and R^{10} are defined as combined to form an oxo group. This is vague and confusing.

Claim 28 is vague and indefinite in that the claim provides for the use of claimed compounds, but the claim does not set forth any steps involved in determining which are the diseases capable of being modulated by calcium receptor. Determining whether a given disease responds or does not respond to such an inhibitor will involve undue experimentation. Suppose that a given drug, which has inhibitor properties in vitro, when administered to a patient with a certain disease, does not produce a favorable response. One cannot conclude that specific disease does not fall within this claim. Keep in mind that:

A. It may be that the next patient will respond. No pharmaceutical has 100% efficacy. What success rate is required to conclude our drug is a treatment? Thus, how many patients need to be treated? If "successful treatment" is what is intended, what criterion is to be used? If one person in 10 responds to a given drug, does that mean that the disease is treatable? One in 100? 1,000? 10,000? Will the standard vary depending on the current therapy for the disease?

B. It may be that the wrong dosage or dosage regimen was employed. Drugs with similar chemical structures can have markedly different pharmacokinetics and metabolic fates. It is quite common for pharmaceuticals to work and or be safe at one dosage, but not at another that is significantly higher or lower. Furthermore, the dosage regimen may be vital --- should the drug be given e.g. once a day, or four times in divided dosages? The optimum route of administration cannot be predicted in advance. Should our drug be given as a bolus iv or in a time release po formulation. Thus, how many dosages and dosage regimens must be tried before one is certain that our drug is not a treatment for this specific disease?

C. It may be that our specific drug, while active in vitro, simply is not potent enough or produces such low concentrations in the blood that it is not an effective treatment of the specific disease. Perhaps a structurally related drug is potent enough or produces high enough blood concentrations to treat the disease in question, so that the first drug really does fall within the claim. Thus, how many different structurally related inhibitors must be tried before one concludes that a specific compound does not fall within the claim?

D. Conversely, if the disease responds to our second drug but not to the first, both of which are inhibitors in vitro, can one really conclude that the disease falls within the claim? It may be that the first compound result is giving the accurate answer, and that the success of second compound arises from some other unknown property, which the second drug is capable. It is common for a drug, particularly in bone diseases, to work by many mechanisms. The history of psychopharmacology is filled with drugs, which were claimed to be a pure receptor XYX agonist or antagonist, but upon further experimentation shown to affect a variety of biological targets. In fact, the development of a drug for a specific disease and the determination of its biological site of action usually precede linking that site of action with the disease. Thus, when mixed results are obtained, how many more drugs need be tested?

E. Suppose that our drug is an effective treatment of the disease of interest, but only when combined with some totally different drug. There are for example, agents in antiviral and anticancer chemotherapy, which are not themselves effective, but are effective treatments when the agents are combined with something else.

Consequently, determining the true scope of the claim will involve extensive and potentially inconclusive research. Without it, one skilled in the art cannot determine the actual scope of the claim. Hence, the claim is indefinite.

Claims 2, 4-6, 8-18, 32, 33 and 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds of Formula 1, wherein R^1= alkyl, aralkyl, C(O) and $S(O)_2$, R^2 is hydrogen, alkyl, alkylthio and alkoxy, Ar= cyclic, X= CH, Y= CH, R^9 and R^{10}= hydrogen, alkyl, aralkyl, and phenyl and R^3= aralkyl, hydrogen and alkyl does not reasonably provide enablement for compounds of Formula 1, wherein R^1 is H, an optionally substituted hydrocarbon group, an optionally substituted hydroxyl group, an optionally substituted thiol group, an optionally substituted amino group, cyano group, a halogen atom, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ is -CO-, -CS-, - SO- or $-SO^2-$, and Z^2 is an optionally substituted hydrocarbon group, an optionally substituted heterocyclic group, an optionally substituted hydroxyl group, or an optionally substituted amino group); R^3 is H, an optionally substituted hydrocarbon group, an optionally substituted hydroxyl group, an optionally substituted amino group, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ and Z^2 are as defined above); Y is C, CR^4 (wherein R^4 is H, an optionally substituted hydrocarbon group, an optionally substituted hydroxyl group, an optionally substituted amino group, an optionally substituted thiol group, cyano group, a halogen atom, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ and Z^2 are as defined above)); R8 is H, an optionally substituted hydrocarbon group, an optionally substituted hydroxyl group, an optionally substituted amino group, an optionally substituted thiol

group, cyano group, a halogen atom, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ and Z^2 are as defined above); R^9 and R^{10} are the same or different and are an optionally substituted hydroxyl group, an optionally substituted amino group, an optionally substituted thiol group, cyano group, a halogen atom, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ and Z^2 are as defined above), or R^9 and R^{10} may be combined to form an oxo group, methylene group or a ring; X^3 is an optionally substituted bivalent [[C_{1-2}]] C_1 hydrocarbon group. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Pursuant to In re Wands, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see In re Vaeck, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(A) Breadth of claims: Scope of the compounds. Owing to the range of many variables, trillions of substituted pyrazolo[1,5-a]pyrimidines are embraced.

(B) The nature of the invention: The invention is a highly substituted pyrazolo[1,5-a]pyrimidines.

(C) Level of predictability in the art: It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(D) Direction or Guidance: That provided is very limited. Applicant shows a general synthesis of compounds of Formula 1, under Preparation on pages 102-132 of the Specification, but does not show the starting material used to make the variety of compounds claimed. There is limited evidence in the Specification of the example compounds that only cover a small portion of the substituents claimed of Formula 1. Thus, there is no specific direction or guidance regarding said compounds of Formula 1 specifically mentioned in Scope.

The specification does not provide any support for the synthesis of compounds of Formula 1, wherein R^1 is H, an optionally substituted hydrocarbon group, an optionally substituted hydroxyl group, an optionally substituted thiol group, an optionally substituted amino group, cyano group, a halogen atom, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ is -CO-, -CS-, - SO- or $-SO^2-$, and Z^2 is an optionally substituted hydrocarbon group, an optionally substituted heterocyclic group, an optionally substituted hydroxyl group, or an optionally substituted amino group); R^3 is H, an optionally substituted hydrocarbon group, an optionally substituted hydroxyl group, an optionally substituted amino group, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ and Z^2 are as

defined above); Y is C, CR^4 (wherein R^4 is H, an optionally substituted hydrocarbon group, an optionally substituted hydroxyl group, an optionally substituted amino group, an optionally substituted thiol group, cyano group, a halogen atom, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ and Z^2 are as defined above)); R^8 is H, an optionally substituted hydrocarbon group, an optionally substituted hydroxyl group, an optionally substituted amino group, an optionally substituted thiol group, cyano group, a halogen atom, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ and Z^2 are as defined above); R^9 and R^{10} are the same or different and are an optionally substituted hydroxyl group, an optionally substituted amino group, an optionally substituted thiol group, cyano group, a halogen atom, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ and Z^2 are as defined above), or R^9 and R^{10} may be combined to form an oxo group, methylene group or a ring; X^3 is an optionally substituted bivalent [[C_{1-2}]] C_1 hydrocarbon group.

The availability of the starting material that is needed to prepare the invention as claimed is at issue here...As per MPEP 21'64.01 (b). A key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to a make the invention are available. In the biotechnical area, this is often true when the product or process requires a particular strain of microorganism and when the microorganism is available only after extensive screening. The Court in *In re Ghiron*, 442 F.2d 985, 991,169 USPQ 723, 727 (CCPA 1971), made it clear that if the practice of a method requires a particular apparatus, the application must provide a sufficient disclosure of the apparatus if the apparatus is not readily available. The same can be said if certain chemicals are required to make a compound or practice a chemical process. *In re Howarth*, 654 F.2d 103, 105, 210 USPQ 689, 691 (CCPA 1981).

(E) State of the Prior Art: These compounds are substituted pyrazolo[1,5-a]pyrimidines of Formula I wherein R^1= alkyl, aralkyl, C(O) and $S(O)_2$, R^2 is hydrogen, alkyl, alkylthio and alkoxy, Ar= cyclic, X= CH, Y= CH, R^9 and R^{10}= hydrogen, alkyl, aralkyl, and phenyl and R^3= aralkyl, hydrogen and alkyl which are well documented in the art. So far as the examiner is aware, no substituted pyrazolo[1,5-a]pyrimidines of Formula I wherein R^1 is H, an optionally substituted hydrocarbon group, an optionally substituted hydroxyl group, an optionally substituted thiol group, an optionally substituted amino group, cyano group, a halogen atom, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ is -CO-, -CS-, - SO- or $-SO^2-$, and Z^2 is an optionally substituted hydrocarbon group, an optionally substituted heterocyclic group, an optionally substituted hydroxyl group, or an optionally substituted amino group); R^3 is H, an optionally substituted hydrocarbon group, an optionally substituted hydroxyl group, an optionally substituted amino group, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ and Z^2 are as defined above); Y is C, CR^4 (wherein R^4 is H, an optionally substituted hydrocarbon group, an optionally substituted hydroxyl group, an optionally substituted amino group, an optionally substituted thiol group, cyano group, a halogen atom, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ and Z^2 are as defined above)); R^8 is H, an optionally substituted hydrocarbon group, an optionally substituted hydroxyl group, an optionally substituted amino group, an optionally substituted thiol group, cyano group, a halogen atom, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ and Z^2 are as defined above); R^9 and R^{10} are the same or different and are an optionally substituted hydroxyl group, an optionally substituted amino group, an optionally

substituted thiol group, cyano group, a halogen atom, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ and Z^2 are as defined above), or R^9 and R^{10} may be combined to form an oxo group, methylene group or a ring; X^3 is an optionally substituted bivalent [[C_{1-2}]] C_1 hydrocarbon group of any kind have been made or used.

(F) Working Examples: Applicant shows example 1-923 and 1143-1146 but no working examples were shown of Formula I wherein R^1 is H, an optionally substituted hydrocarbon group, an optionally substituted hydroxyl group, an optionally substituted thiol group, an optionally substituted amino group, cyano group, a halogen atom, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ is -CO-, -CS-, - SO- or $-SO^2-$, and Z^2 is an optionally substituted hydrocarbon group, an optionally substituted heterocyclic group, an optionally substituted hydroxyl group, or an optionally substituted amino group); R^3 is H, an optionally substituted hydrocarbon group, an optionally substituted hydroxyl group, an optionally substituted amino group, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ and Z^2 are as defined above); Y is C, CR^4 (wherein R^4 is H, an optionally substituted hydrocarbon group, an optionally substituted hydroxyl group, an optionally substituted amino group, an optionally substituted thiol group, cyano group, a halogen atom, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ and Z^2 are as defined above)); R^8 is H, an optionally substituted hydrocarbon group, an optionally substituted hydroxyl group, an optionally substituted amino group, an optionally substituted thiol group, cyano group, a halogen atom, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ and Z^2 are as defined above); R^9 and R^{10} are the same or different and an optionally

substituted hydroxyl group, an optionally substituted amino group, an optionally substituted thiol group, cyano group, a halogen atom, an optionally substituted heterocyclic group, or a group of the formula: $-Z^1-Z^2$ (wherein $-Z^1-$ and Z^2 are as defined above), or R^9 and R^{10} may be combined to form an oxo group, methylene group or a ring; X^3 is an optionally substituted bivalent [[C_{1-2}]] C_1 hydrocarbon group of any kind have been made or used.

(G) Skill of those in the art: The ordinary artisan is highly skilled.

(H) The quantity of experimentation needed: Since there are very limited working examples as described above, the amount of experimentation is expected to be high and burdensome.

Due to the level of unpredictability in the art, the very limited guidance provide, and the lack of working examples, the Applicant has shown lack of enablement for the groups noted groups on Formula i. MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Claim 29 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the

specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Such a utility cannot be deemed enabled. .

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(A) Breadth of claims.

(a) Scope of the compounds. Owing to the range of 5 primary variables, trillions pyrazolo[1,5-a]pyrimidine compounds are embraced.

(b) Scope of the diseases covered. Claim 29 is drawn to a method of treating bone diseases. A list of bone diseases, includes, but is not limited to: Bone cyst, Bone spur (Osteophytes), Bone tumor, Craniosynostosis, Fibrodysplasia ossificans progressiva, Fibrous dysplasia, Giant cell tumor of bone, Hypophosphatasia, Klippel-Feil syndrome, Metabolic Bone Disease, Osteitis deformans (or Paget's disease of bone), Osteitis fibrosa cystica (or Osteitis fibrosa, or Von Recklinghausen's disease of bone), Osteitis pubis, Condensing osteitis (or Osteitis condensans), Osteitis condensans ilii, Osteochondritis dissecans, Osteochondroma (Bone Tumor), Osteogenesis Imperfecta,

Osteomalacia, Osteomyelitis, Osteopenia, Osteopetrosis, Osteoporosis, Osteosarcoma (Bone Tumor), Porotic hyperostosis, Primary hyperparathyroidism and Renal Osteodystrophy.

(B) The nature of the invention and predictability in the art: The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(C) Direction or Guidance: That provided is very limited. The dosage range information 0.1 mg—10 mg 1-3 times daily is on page 135 of the Specification. Moreover, this is generic, the same for the many disorders covered by the specification. Thus, there is no specific direction or guidance regarding a regimen or dosage effective specifically for the treatment of bone diseases.

(D) State of the Prior Art: These compounds are substituted pyrazolo(1,5-a)pyrimidines. So far as the examiner is aware, no substituted pyrazolo(1,5-a)pyrimidines of any kind have been used for the treatment of bone diseases.

(E) Working Examples: There are seven working examples from a [^{35}S]GTP$_y$S binding pharmacological assay on page 428 of the Specification. There are no working examples drawn to the treatment of any bone disease in the form of animal models.

(F) Skill of those in the art: These diseases and disorders covered by the Scope of diseases above cannot be treated generally by any one drug. These are all different diseases and disorders, which occur at different locations and by different modes of action in the body.

Note there are some diseases listed in the Scope of diseases which cannot be treated with pharmaceuticals. For example, osteopetrosis, also known as marble bone disease, is an extremely rare inherited disorder whereby the bones harden, becoming denser, in contrast to the more prevalent osteomalacia, in which the bones soften.

(G) The quantity of experimentation needed: Owing especially to factors A, C, E and F, the amount of experimentation is expected to be high.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 2, 5, 6 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Bellec et. al. (J. Het. Chem., 1995, 32(6), 1793-1800).

The reference teaches compounds of formula (I), wherein R^1= methyl, R^3= hydrogen, Ar= phenyl, R^8= methyl, R^9= hydrogen, R^{10}= phenyl, X3= CH and the bond between X and Y is a double bond. See compound 2i, on page 1795, table 3. Furthermore, all of the species in table 3 anticipate said claims.

Claims 2, 4-6 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Reddy et. al. (Ind. J. Chem., 1993, 32B(5), 586-589).

The reference teaches compounds of formula (I), wherein R^1= $C(O)NH_2$, R^3= hydrogen, Ar= phenyl, R^8= hydrogen, R^9= methyl, R^{10}= phenyl, X3= CH and the bond between X and Y is a double bond. See compound 2e, on page 587, table 1. Furthermore, all of the species in table 1 anticipate said claims.

Claims 2, 5, 6 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Tsuda et. al. (U.S. 4918074).

The reference teaches compounds of formula (I), wherein R^1= hydrogen, R^3= hydrogen, Ar= 2-fluorophenyl, R^8= hydrogen, R^9= hydrogen, R^{10}= C(O)OPh, X3= CHC(O)OEt and the bond between X and Y is a double bond. See the CAS printout, accession number 1991:81873, downloaded 1/29/2008. Thus, said claims are anticipated by Tsuda et. al.

Claims 2, 5, 6, 8, 11, 28, 29, 32, 33 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Atwal et. al. (U.S. 4746656).

The reference teaches compounds of formula (I), wherein R^1= hydrogen, R^3= hydrogen, Ar= 2,3-dichlorophenyl, R^8= hydroxyl, R^9= hydrogen, R^{10}= methyl, X3= CHC(O)OEt and the bond between X and Y is a double bond. See column 6, lines 19-22. Also, the specie, wherein R^1= hydrogen, R^3= hydrogen, Ar= 3-nitrophenyl, R^8= hydroxyl, R^9= hydrogen, R^{10}= methyl, X3= CHC(O)Oi-Pro and the bond between X and Y is a double bond. See column 6, lines 26-28. The compositions are taught in column 3, line 36. The reference teaches the compounds as calcium entry blocking vasodialators, see column 2, line 68. There are other species which anticipate said claims. Thus, said claims are anticipated by Atwal et. al.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSANNA MOORE whose telephone number is (571)272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Susanna Moore/
Examiner, Art Unit 1624

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